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<110> Van Mellaert, Herman

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Botterman, Johan
      Van Rie, Jeroen
      Joos, Henk
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tct aac aga ggc tat ggg gat tac aca cca cta ccg gct ggt tat gta Ser Asn Arg Gly Tyr Gly Asp Tyr Thr Pro Leu Pro Ala Gly Tyr Val 1140 1145 1150	3692
aca aag gat tta gag tac ttc cca gag acc gat aag gta tgg att gag Thr Lys Asp Leu Glu Tyr Phe Pro Glu Thr Asp Lys Val Trp Ile Glu 1155 1160 1165	3740
atc gga gaa aca gaa gga aca ttc atc gtg gat agc gtg gaa tta ctc Ile Gly Glu Thr Glu Gly Thr Phe Ile Val Asp Ser Val Glu Leu Leu 1170 1175 1180 1185	3788
ctt atg gag gaa taa gatacgttat aaaatgtaac gtatgcaaat aaagaatgat Leu Met Glu Glu 1190	3843
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Ser Ser Ile Asp Ile Ser Leu Ser Leu Val Gln Phe Met Val Ser Asn 35 40 45

Phe Val Pro Gly Gly Gly Phe Leu Val Gly Leu Ile Asp Phe Val Trp 50 55 60

Gly Ile Val Gly Pro Ser Gln Trp Asp Ala Phe Leu Val Gln Ile Glu
65 70 75 80

Gln Leu Ile Asn Glu Arg Ile Ala Glu Phe Ala Arg Asn Ala Ala Ile 85 90 95

Ala Asn Leu Glu Gly Leu Glu Asn Asn Leu Asn Ile Tyr Val Glu Ala 100 105 110

Phe Lys Glu Trp Glu Glu Asp Pro Asn Asn Pro Glu Thr Arg Thr Arg 115 120 125

Val Ile Asp Arg Phe Arg Ile Leu Asp Gly Leu Leu Glu Arg Asp Ile 130 135 140

Ala Gln Ala Ala Asn Leu His Leu Ala Ile Leu Arg Asp Ser Val Ile 165 170 175

Phe Gly Glu Arg Trp Gly Leu Thr Thr Ile Asn Val Asn Glu Asn Tyr 180 185 190

Asn Arg Leu Ile Arg His Ile Asp Glu Tyr Ala Asp His Cys Ala Asn 195 200 205

Thr Tyr Asn Arg Gly Leu Asn Asn Leu Pro Lys Ser Thr Tyr Gln Asp 210 215 220

Trp Ile Thr Tyr Asn Arg Leu Arg Arg Asp Leu Thr Leu Thr Val Leu 225 230 235 240

Asp Ile Ala Ala Phe Phe Pro Asn Tyr Asp Asn Arg Arg Tyr Pro Ile
245 250 255

Gln Pro Val Gly Gln Leu Thr Arg Glu Val Tyr Thr Asp Pro Leu Ile 260 265 270

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Tyr	Trp	Gly	Gly	His 325	Arg	Val	Ile	Ser	Ser 330	Leu	Ile	Gly	Gly	Gly 335	Asn
Ile	Thr	Ser	Pro 340	Ile	Tyr	Gly	Arg	Glu 345	Ala	Asn	Gln	Glu	Pro 350	Pro	Arg
Ser	Phe	Thr 355	Phe	Asn	Gly	Pro	Val 360	Phe	Arg	Thr	Leu	Ser 365	Asn	Pro	Thr
Leu	Arg 370	Leu	Leu	Gln	Gln	Pro 375	Trp	Pro	Ala	Pro	Pro 380	Phe	Asn	Leu	Arg
Gly 385	Val	Glu	Gly	Val	Glu 390	Phe	Ser	Thr	Pro	Thr 395	Asn	Ser	Phe	Thr	Tyr 400
Arg	Gly	Arg	Gly	Thr 405	Val	Asp	Ser	Leu	Thr 410	Glu	Leu	Pro	Pro	Glu 415	Asp
Asn	Ser	Val	Pro 420	Pro	Arg	Glu	Gly	Tyr 425	Ser	His	Arg	Leu	Cys 430	His	Ala
Thr	Phe	Val 435	Gln	Arg	Ser	Gly	Thr 440	Pro	Phe	Leu	Thr	Thr 445	Gly	Val	Val
Phe	Ser 450	Trp	Thr	His	Arg	Ser 455	Ala	Thr	Leu	Thr	Asn 460	Thr	Ile	Asp	Pro
Glu 465	Arg	Ile	Asn	Gln	Ile 470	Pro	Leu	Val	Lys	Gly 475	Phe	Arg	Val	Trp	Gly 480
Gly	Thr	Ser	Val	Ile 485	Thr	Gly	Pro	Gly	Phe 490	Thr	Gly	Gly	Asp	Ile 495	Leu
Arg	Arg	Asn	Thr 500	Phe	Gly	Asp	Phe	Val 505	Ser	Leu	Gln	Val	Asn 510	Ile	Asn
Ser	Pro	Ile 515	Thr	Gln	Arg	Tyr	Arg 520	Leu	Arg	Phe	Arg	Tyr 525	Ala	Ser	Ser
Arg	Asp 530	Ala	Arg	Val	Ile	Val 535	Leu	Thr	Gly	Ala	Ala 540	Ser	Thr	Gly	Val

Gly 545	Gly	Gln	Val	Ser	Val 550	Asn	Met	Pro	Leu	Gln 555	Lys	Thr	Met	Glu	Ile 560
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Pro	Phe	Ser	Phe 580	Arg	Ala	Asn	Pro	Asp 585	Ile	Ile	Gly	Ile	Ser 590	Glu	Gln
Pro	Leu	Phe 595	Gly	Ala	Gly	Ser	Ile 600	Ser	Ser	Gly	Glu	Leu 605	Tyr	Ile	Asp
Lys	Ile 610	Glu	Ile	Ile	Leu	Ala 615	Asp	Ala	Thr	Phe	Glu 620	Ala	Glu	Ser	Asp
Leu 625	Glu	Arg	Ala	Gln	Lys 630	Ala	Val	Asn	Ala	Leu 635	Phe	Thr	Ser	Ser	Asn 640
Gln	Ile	Gly	Leu	Lys 645	Thr	Asp	Val	Thr	Asp 650	Tyr	His	Ile	Asp	Gln 655	Val
Ser	Asn	Leu	Val 660	Asp	Сув	Leu	Ser	Asp 665	Glu	Phe	Cys	Leu	Asp 670	Glu	Lys
Arg	Glu	Leu 675	Ser	Glu	Lys	Val	Lys 680	His	Ala	Lys	Arg	Leu 685	Ser	Asp	Glu
Arg	Asn 690	Leu	Leu	Gln	Asp	Pro 695	Asn	Phe	Arg	Gly	Ile 700	Asn	Arg	Gln	Pro
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Asp	Val	Phe	Lys	Glu 725	Asn	Tyr	Val	Thr	Leu 730	Pro	Gly	Thr	Val	Asp 735	Glu
Cys	Tyr	Pro	Thr 740	Tyr	Leu	Tyr	Gln	Lys 745	Ile	Asp	Glu	Ser	Lys 750	Leu	Lys
Ala	Tyr	Thr 755	Arg	Tyr	Glu	Leu	Arg 760	Gly	Tyr	Ile	Glu	Asp 765	Ser	Gln	Asp
Leu	Glu 770	Ile	Tyr	Leu	Ile	Arg 775	Tyr	Asn	Ala	Lys	His 780	Glu	Ile	Val	Asn
Val 785	Pro	Gly	Thr	Gly	Ser 790	Leu	Trp	Pro	Leu	Ser 795	Ala	Gln	Ser	Pro	Ile 800
Gly	Lys	Сув	Gly	Glu 805	Pro	Asn	Arg	Cys	Ala 810	Pro	His	Leu	Glu	Trp 815	Asn

Pro Asp Leu Asp Cys Ser Cys Arg Asp Gly Glu Lys Cys Ala His His Ser His His Phe Thr Leu Asp Ile Asp Val Gly Cys Thr Asp Leu Asn Glu Asp Leu Gly Val Trp Val Ile Phe Lys Ile Lys Thr Gln Asp Gly His Ala Arg Leu Gly Asn Leu Glu Phe Leu Glu Glu Lys Pro Leu Leu Gly Glu Ala Leu Ala Arg Val Lys Arg Ala Glu Lys Lys Trp Arg Asp Lys Arg Glu Lys Leu Gln Leu Glu Thr Asn Ile Val Tyr Lys Glu Ala Lys Glu Ser Val Asp Ala Leu Phe Val Asn Ser Gln Tyr Asp Arg Leu Gln Val Asp Thr Asn Ile Ala Met Ile His Ala Ala Asp Lys Arg Val His Arg Ile Arg Glu Ala Tyr Leu Pro Glu Leu Ser Val Ile Pro Gly Val Asn Ala Ile Phe Glu Glu Leu Glu Gly Arg Ile Phe Thr Ala Tyr Ser Leu Tyr Asp Ala Arg Asn Val Ile Lys Asn Gly Asp Phe Asn Asn Gly Leu Leu Cys Trp Asn Val Lys Gly His Val Asp Val Glu Glu Gln Asn Asn His Arg Ser Val Leu Val Ile Pro Glu Trp Glu Ala Glu Val Ser Gln Glu Val Arg Val Cys Pro Gly Arg Gly Tyr Ile Leu Arg Val Thr Ala Tyr Lys Glu Gly Tyr Gly Glu Gly Cys Val Thr Ile His Glu Ile Glu Asp Asn Thr Asp Glu Leu Lys Phe Ser Asn Cys Val Glu Glu Glu Val Tyr Pro Asn Asn Thr Val Thr Cys Asn Asn Tyr Thr Gly

Thr Gln Glu Glu 1 1090	yr Glu Gly Thr 1095	Tyr Thr Ser Arg Asn Gln 1100	Gly Tyr
Asp Glu Ala Tyr G	Sly Asn Asn Pro 1110	Ser Val Pro Ala Asp Tyr 1115	Ala Ser 1120
	ys Ser Tyr Thr 25	Asp Gly Arg Arg Glu Asn 1130 1	Pro Cys 135
Glu Ser Asn Arg G 1140	Gly Tyr Gly Asp	Tyr Thr Pro Leu Pro Ala 1145 1150	Gly Tyr
Val Thr Lys Asp L 1155	eu Glu Tyr Phe 1160	Pro Glu Thr Asp Lys Val 1165	Trp Ile
Glu Ile Gly Glu T 1170	Thr Glu Gly Thr 1175	Phe Ile Val Asp Ser Val 1180	Glu Leu
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Val	Gly	Glu	Leu	Trp 85	Pro	Arg	Gly	Arg	Asp 90	Gln	Trp	Glu	Ile	Phe 95	Leu	
		gtc Val	_									_		_		336
		gct Ala 115		-	_					_						384
		cag Gln			_	_			_		_	_	_	_	-	432
_	_	agt Ser	_							_		_		_		480
		gcg Ala	_	_			_					_	_			528
_	_	gta Val		_		_	_							_	_	576
		tct Ser 195														624
		tat Tyr														672
		gta Val														720
		gca Ala														768
		gta Val		_			_				_					816
		cca Pro 275			_	_	_	_			_	-	_			864
		att Ile														912

•

290 295 300

aat Asn 305	aat Asn	aat Asn	gca Ala	cct Pro	tcg Ser 310	ttc Phe	tct Ser	gcc Ala	ata Ile	gag Glu 315	gct Ala	gcg Ala	gct Ala	Ile	cga Arg 320	960
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tta Leu 465	Ser	cat His	ata Ile	ggt Gly	ata Ile 470	Ile	tta Leu	caa Gln	tcc Ser	agg Arg 475	y Val	g aat . Asn	gta Val	ccg Pro	gta Val 480	1440
tat Tyr	tct Ser	tgg Trp	acg Thr	cat His	Arg	agt Ser	gca Ala	gat Asp	cgt Arc 490	y Thi	g aat Asr	acg Thr	att Ile	gga Gly 495	cca Pro	1488
aat Asr	aga n Arg	ato J Ile	acc Thr	Glr	ato lle	cca Pro	ato Met	g gta Val	l Lys	a gca s Ala	a tco a Sei	gaa Glu	ctt Leu 510	Pro	caa Gln	1536

					aga Arg											1584
_	_				ggt Gly											1632
					aga Arg 550											1680
					ttt Phe											1728
					aca Thr											1776
					gct Ala											1824
					acg Thr											1872
					att Ile 630											1920
					gaa Glu											1968
					aga Arg											2016
					aat Asn											2064
					gaa Glu											2112
					aac Asn 710											2160
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ccg Pro	ggt Gly 770	act Thr	ttt Phe	aat Asn	gag Glu	tgt Cys 775	tat Tyr	ccg Pro	acg Thr	tat Tyr	tta Leu 780	tat Tyr	caa Gln	aaa Lys	ata Ile	2352
ggg Gly 785	gag Glu	tcg Ser	gaa Glu	tta Leu	aaa Lys 790	gct Ala	tat Tyr	act Thr	cgc Arg	tac Tyr 795	caa Gln	tta Leu	aga Arg	ggt Gly	tat Tyr 800	2400
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tca Ser	gtt Val	gaa Glu 835	Ser	cca Pro	atc Ile	gga Gly	agg Arg 840	tgc Cys	gga Gly	gaa Glu	ccg Pro	aat Asn 845	cga Arg	tgc Cys	gca Ala	2544
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gaa Glu 865	aaa Lys	tgt Cys	gcg Ala	cat His	cat His 870	tcc Ser	cat His	cat His	ttc Phe	tct Ser 875	Leu	gat Asp	att Ile	gat Asp	gtt Val 880	2640
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att Ile	aag Lys	acg Thr	g cag Gln 900	Glu	ggt Gly	cat His	gca Ala	aga Arg 905	Leu	ggg Gly	aat Asn	ctg Leu	gaa Glu 910	Phe	att : Ile	2736
gaa Glu	gag Glu	aaa Lys 915	Pro	tta Leu	tta Leu	gga Gly	gaa Glu 920	ı Ala	ctg Lev	g tct Ser	cgt Arg	gtg Val 925	Lys	g agg s Arg	gga gAla	2784
gaç Glü	g aaa Lys	a aaa s Lys	a tgg s Trp	g aga Arg	gac J Asp	aaa Lys	cgt Arg	gaa g Glu	a aaa 1 Lys	a cta Lei	a caa a Glr	a ttg 1 Leu	gaa Glu	aca ı Thr	a aaa Lys	2832

930 935 940

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gcg gca gat aaa ctt gtt cat cga att cga gag gcg tat ctt tca gaa Ala Ala Asp Lys Leu Val His Arg Ile Arg Glu Ala Tyr Leu Ser Glu 980 985 990	2976
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ggt cac att atc act gca atc tcc tta tac gat gcg aga aat gtc Gly His Ile Ile Thr Ala Ile Ser Leu Tyr Asp Ala Arg Asn Val 1010 1015 1020	3069
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gct Ala	ggt Gly 1190	tat Tyr	gtg Val	aca Thr	aaa Lys	gaa Glu 1195	Leu	gaa Glu	tac Tyr	ttc Phe	cca Pro 1200	Glu	aca Thr	gat Asp	3609
	gta Val 1205	tgg Trp	att Ile	gag Glu	att Ile	gga Gly 1210	Glu	acg Thr	gaa Glu	a gga ı Gly	aag Lys 1215	Phe	att Ile	gta Val	3654
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Asn	n His	Ser	Ala 20	Gln	Met	Asp l		Leu 1 25	Pro .	Asp A	Ala A	rg Il 30		u Asp	
Sei	Leu	Cys 35	Ile	Ala	Glu		Asn A	Asn	Ile	Asp :	Pro P 4		ıl Se	er Ala	
Sei	Thr 50	Val	Gln	Thr	Gly	Ile . 55	Asn	Ile	Ala		Arg I 60	le Le	eu Gl	ly Val	
Le: 65	ı Gly	Val	Pro	Phe	Ala 70	Gly	Gln	Leu	Ala	Ser 75	Phe T	yr Se	er Pl	ne Leu 80	

Val Gly Glu Leu Trp Pro Arg Gly Arg Asp Gln Trp Glu Ile Phe Leu

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Tyr Gln Gln Ser Leu Glu Asp Trp Leu Glu Asn Arg Asp Asp Ala Arg 130 135 140

Thr Arg Ser Val Leu His Thr Gln Tyr Ile Ala Leu Glu Leu Asp Phe 145 150 155 160

Leu Asn Ala Met Pro Leu Phe Ala Ile Arg Asn Gln Glu Val Pro Leu 165 170 175

Leu Met Val Tyr Ala Gln Ala Ala Asn Leu His Leu Leu Leu Leu Arg 180 185 190

Asp Ala Ser Leu Phe Gly Ser Glu Phe Gly Leu Thr Ser Gln Glu Ile 195 200 205

Gln Arg Tyr Tyr Glu Arg Gln Val Glu Arg Thr Arg Asp Tyr Ser Asp 210 215 220

Tyr Cys Val Glu Trp Tyr Asn Thr Gly Leu Asn Ser Leu Arg Gly Thr 225 230 235 235

Asn Ala Ala Ser Trp Val Arg Tyr Asn Gln Phe Arg Arg Asp Leu Thr 245 250 255

Leu Gly Val Leu Asp Leu Val Ala Leu Phe Pro Ser Tyr Asp Thr Arg 260 265 270

Thr Tyr Pro Ile Asn Thr Ser Ala Gln Leu Thr Arg Glu Val Tyr Thr 275 280 285

Asp Ala Ile Gly Ala Thr Gly Val Asn Met Ala Ser Met Asn Trp Tyr 290 295 300

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Ser	Ser	Arg	Trp 340	Ser	Asn	Thr	Arg	His 345	Met	Thr	Tyr	Trp	Arg 350	Gly	His
Thr	Ile	Gln 355	Ser	Arg	Pro	Ile	Gly 360	Gly	Gly	Leu	Asn	Thr 365	Ser	Thr	His
Gly	Ala 370	Thr	Asn	Thr	Ser	Ile 375	Asn	Pro	Val	Thr	Leu 380	Arg	Phe	Ala	Ser
Arg 385	Asp	Val	Tyr	Arg	Thr 390	Glu	Ser	Tyr	Ala	Gly 395	Val	Leu	Leu	Trp	Gly 400
Ile	Tyr	Leu	Glu	Pro 405	Ile	His	Gly	Val	Pro 410	Thr	Val	Arg	Phe	Asn 415	Phe
Thr	Asn	Pro	Gln 420	Asn	Ile	Ser	Asp	Arg 425	Gly	Thr	Ala	Asn	Tyr 430	Ser	Gln
Pro	Tyr	Glu 435	Ser	Pro	Gly	Leu	Gln 440	Leu	Lys	Asp	Ser	Glu 445	Thr	Glu	Leu
Pro	Pro 450	Glu	Thr	Thr	Glu	Arg 455	Pro	Asn	Tyr	Glu	Ser 460	Tyr	Ser	His	Arg
Leu 465	Ser	His	Ile	Gly	Ile 470	Ile	Leu	Gln	Ser	Arg 475	Val	Asn	Val	Pro	Val 480
Tyr	Ser	Trp	Thr	His 485	Arg	Ser	Ala	Asp	Arg 490	Thr	Asn	Thr	Ile	Gly 495	Pro
Asn	Arg	Ile	Thr 500	Gln	Ile	Pro	Met	Val 505	Lys	Ala	Ser	Glu	Leu 510	Pro	Gln

• ...

Gly Thr Thr Val Val Arg Gly Pro Gly Phe Thr Gly Gly Asp Ile Leu 520 515 Arg Arg Thr Asn Thr Gly Gly Phe Gly Pro Ile Arg Val Thr Val Asn 535 530 Gly Pro Leu Thr Gln Arg Tyr Arg Ile Gly Phe Arg Tyr Ala Ser Thr 555 560 550 545 Val Asp Phe Asp Phe Phe Val Ser Arg Gly Gly Thr Thr Val Asn Asn 570 565 Phe Arg Phe Leu Arg Thr Met Asn Ser Gly Asp Glu Leu Lys Tyr Gly 585 580 Asn Phe Val Arg Arg Ala Phe Thr Thr Pro Phe Thr Phe Thr Gln Ile 595 600 605 Gln Asp Ile Ile Arg Thr Ser Ile Gln Gly Leu Ser Gly Asn Gly Glu 615 Val Tyr Ile Asp Lys Ile Glu Ile Ile Pro Val Thr Ala Thr Phe Glu 635 630 625 Ala Glu Tyr Asp Leu Glu Arg Ala Gln Glu Ala Val Asn Ala Leu Phe 645 650 655 Thr Asn Thr Asn Pro Arg Arg Leu Lys Thr Asp Val Thr Asp Tyr His 665 670 Ile Asp Gln Val Ser Asn Leu Val Ala Cys Leu Ser Asp Glu Phe Cys 685 680 675 Leu Asp Glu Lys Arg Glu Leu Leu Glu Lys Val Lys Tyr Ala Lys Arg 695 700 690 Leu Ser Asp Glu Arg Asn Leu Leu Gln Asp Pro Asn Phe Thr Ser Ile 710 715 720 Asn Lys Gln Pro Asp Phe Ile Ser Thr Asn Glu Gln Ser Asn Phe Thr Ser Ile His Glu Gln Ser Glu His Gly Trp Trp Gly Ser Glu Asn Ile 740 745 750

Thr Ile Gln Glu Gly Asn Asp Val Phe Lys Glu Asn Tyr Val Thr Leu 755 760 765

Pro Gly Thr Phe Asn Glu Cys Tyr Pro Thr Tyr Leu Tyr Gln Lys Ile 770 775 780

Gly Glu Ser Glu Leu Lys Ala Tyr Thr Arg Tyr Gln Leu Arg Gly Tyr 785 790 795 800

Ile Glu Asp Ser Gln Asp Leu Glu Ile Tyr Leu Ile Arg Tyr Asn Ala 805 810 815

Lys His Glu Thr Leu Asp Val Pro Gly Thr Glu Ser Leu Trp Pro Leu 820 825 830

Ser Val Glu Ser Pro Ile Gly Arg Cys Gly Glu Pro Asn Arg Cys Ala 835 840 845

Pro His Phe Glu Trp Asn Pro Asp Leu Asp Cys Ser Cys Arg Asp Gly 850 855

Glu Lys Cys Ala His His Ser His His Phe Ser Leu Asp Ile Asp Val 865 870 875 880

Gly Cys Thr Asp Leu His Glu Asn Leu Gly Val Trp Val Val Phe Lys 885 890 895

Ile Lys Thr Gln Glu Gly His Ala Arg Leu Gly Asn Leu Glu Phe Ile 900 905 910

Glu Glu Lys Pro Leu Leu Gly Glu Ala Leu Ser Arg Val Lys Arg Ala 915 920 925

Glu Lys Lys Trp Arg Asp Lys Arg Glu Lys Leu Gln Leu Glu Thr Lys 930 935 940

Arg Val Tyr Thr Glu Ala Lys Glu Ala Val Asp Ala Leu Phe Val Asp 945 950 955 960

Ser Gln Tyr Asp Arg Leu Gln Ala Asp Thr Asn Ile Gly Met Ile His 965 970 975

Ala Ala Asp Lys Leu Val His Arg Ile Arg Glu Ala Tyr Leu Ser Glu 980 985 990

Leu Pro Val Ile Pro Gly Val Asn Ala Glu Ile Phe Glu Glu Leu Glu 995 1000 1005

Gly His Ile Ile Thr Ala Ile Ser Leu Tyr Asp Ala Arg Asn Val

Val Lys Asn Gly Asp Phe Asn Asn Gly Leu Thr Cys Trp Asn Val 1025

Lys Gly His Val Asp Val Gln Gln Ser His His Arg Ser Asp Leu 1040 1045 1050

Val Ile Pro Glu Trp Glu Ala Glu Val Ser Gln Ala Val Arg Val 1055 1060 1065

Cys Pro Gly Cys Gly Tyr Ile Leu Arg Val Thr Ala Tyr Lys Glu 1070 1075

Gly Tyr Gly Glu Gly Cys Val Thr Ile His Glu Ile Glu Asn Asn 1085 1090 1095

Thr Asp Glu Leu Lys Phe Lys Asn Arg Glu Glu Glu Glu Val Tyr 1100 1105

Pro Thr Asp Thr Gly Thr Cys Asn Asp Tyr Thr Ala His Gln Gly 1115 1120

Thr Ala Gly Cys Ala Asp Ala Cys Asn Ser Arg Asn Ala Gly Tyr 1130 1135

Ala Sylvania Sylvania

Asp Ser Val Glu Leu Leu Leu Met Glu Glu 1220 1225